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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/700,032	11/03/2003	Hani Sabbah	1059.00096	3424

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EXAMINER

AFREMOVA, VERA

ART UNIT	PAPER NUMBER
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1657

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/06/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary

Application No.

10/700,032

Applicant(s)

SABBAH ET AL.

Examiner

Vera Afremova

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 December 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 2-5 and 8-16 is/are pending in the application.
- 4a) Of the above claim(s) 3-5 and 8-14 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) 2, 15 and 16 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/27/2006 has been entered.

Claims 2,15 and 16 as amended 12/15/2006 are pending and under examination.

Claims 3-5 and 8-14 were withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected groups of inventions. Applicant timely traversed the restriction requirement in the reply filed on 1/18/2006.

Applicants canceled claims 1, 6 and 7.

Claim Rejections - 35 USC § 112

New matter

Claims 2, 15 and 16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Insertion of the limitation "the products consisting essentially of the secretions from the stem cells" in the active step of administering in the method of improving cardiac function has no support in the as-filed specification.

Insertion of the active steps of "separating the stem cells from a supernatant, the supernatant containing products consisting essentially of secretions from the stem cells; and administering the products consisting essentially of the secretions from the stem cells" in the method of improving cardiac function has no support in the as-filed specification.

The insertion of these limitations and active steps is a new concept because they neither have literal support in the as-filed specification by way of a generic disclosure, nor there are specific examples of the newly inserted limitations and active steps that would show possession of the concept of the use of the products "consisting essentially of the secretions from the stem cells" for administering as a sole therapeutic agent without transplantation of stem cells in the method of improving cardiac function.

The generic disclosure of the as-filed specification indicates that "the purpose of the present invention is to utilize stem cells, supernatant from stem cells, the secretions resulting from the interaction of stem cells and other cells (e.g., stem cell products), or compounds that increase the amount of secretions present at a site, for treating heart failure" (specification page 4, lines 23-26). The as-filed specification teaches that the stem cells produce products at the site of administration, thereby, enhancing cellular function (specification page 9, lines 15-21).

Thus, the generic disclosure relates to the potential benefits of the stem cells in combinations with their secretions but not to the secretions alone as a sole therapeutic agent. The as-filed specification does not contain description of an *in vivo* administration of a sole product "consisting essentially of the secretions from the stem cells" to the patient in the method of improving cardiac function. The literal support is also missing for the phrase and/or term "products consisting essentially of the secretions from the stem cells".

The exemplified disclosure relates to an *in vitro* culturing of bone marrow cells and observing expression of factors (page 23). The exemplified disclosure of the active step of “administering the products consisting essentially of the secretions from the stem cells” in the method of improving cardiac function is lacking in the as-filed specification.

Therefore, there is no sufficient support for the newly inserted limitations and active steps as drawn to an *in vivo* administration of stem cell secretions as a sole therapeutic agent to the patient for improving cardiac function.

With regard to the active step of “separating the stem cells from a supernatant” Applicants argue that one of skill in the art would have known how to obtain and to separate a supernatant from the stem cells (response page 6, par. 4). However, the instant rejection is a matter of a written description, not a question of what one of skill in the art would or would not have known. Moreover, the particular example describes that some of the factors that are produced by stem cells (BMSC) in an *in vitro* system and that are also regarded by applicants as beneficial for cardiac function (specification page 7) are not found in the culture medium with the BMSC (specification page 23, lines 26-29). Thus, the structural characteristic of those products that are “consisting essentially of secretions from the stem cells” that would be separated from the stem cells and used as a sole therapeutic agent for *in vivo* administration without transplantation of the stem cells is not contemplated in the as-filed specification. Nor there is a description of a method of administering products “consisting essentially of secretions from the stem cells” as a sole therapeutic agent to the patient for improving cardiac function.

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The material within the four corners of the as-filed specification must lead to the claimed concept. If it does not, the material is new matter. Declarations and new references cannot demonstrate the possession of a concept after the fact.

Thus, the insertion of limitations and active steps of "separating the stem cells from a supernatant, the supernatant containing products consisting essentially of secretions from the stem cells; and administering the products consisting essentially of the secretions from the stem cells" in the method of improving cardiac function is considered to be the insertion of new matter for the above reasons.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 2, 15 and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Pierpaolli et al. (Cellular Immunology. 1981. 57: 219-228)

Claims are directed to a method of improving cardiac function by: a) isolating stem cells from harvested marrow; b) growing the stem cells without differentiation in medium; c) enriching the medium containing the stem cells; d) separating the stem cells from a supernatant, the supernatant containing products consisting essentially of secretions from the stem cells; and e) administering the products consisting essentially of the secretions from the stem cells. Some

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claims are further drawn to the enriching step by exposing to hypoxia. Some claims are further drawn to intravenously administering the products.

Pierpaolli et al. discloses a method comprising steps of a) isolating stem cells from harvested marrow (page 220, last par), b) growing the stem cells without differentiation in medium or storing the cells in the medium (page 220, last par.), c) enriching the medium containing the stem cells under hypoxia or storing cells in a closed vessel in refrigerator (page 220, last par.), d) separating the stem cells from a supernatant, the supernatant containing “products consisting essentially of secretions from the stem cell” that would be “MRF” as disclosed (page 221, par. 2); and e) administering the MRF intravenously (page 221, par. 5 “preconditioning” regiment). The method disclosed by Pierpaolli et al. comprises identical active steps as required by the claimed method and the method disclosed by Pierpaolli et al. comprises identical structural elements within the broadest meaning of the instant claims. Thus, the effect of administration as disclosed by Pierpaolli et al. is reasonably expected to improve cardiac function to at least some degree as encompassed by the claimed invention, particularly in view that the instant specification broadly states that the stem cell products (“products consisting essentially of the secretions from the stem cells” as claimed) can affect cardiac function regardless of the location of administration (specification page 9, line 18-21).

Therefore, the cited reference anticipates the invention as presently claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 2, 15 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 7,097,832 (Kornowski et al).

Claims are directed to a method of improving cardiac function wherein the method comprises steps of culturing bone marrow stem cells and administering products consisting essentially of the secretions from the stem cells. Some claims are further drawn to culturing bone marrow stem cells under hypoxia conditions for enrichment in the secretions from the stem cells. Some claims are further drawn to administering the products to the heart.

US 7,097,832 (Kornowski et al) teaches and/or suggest a method of improving cardiac function wherein the method comprises steps of culturing bone marrow stem cells under hypoxia conditions for enrichment in the secretions from the stem cells (col. 16, lines 45-46; col. 9, lines 1-33) and administering bone marrow stem cells and the bone marrow secretion products (col.17, lines 7-15; col. 15, lines 56-60). The cited US 7,097,832 clearly teaches that the bone marrow secreted factors are necessary to promote new blood vessel growth and to restore function of ischemic heart (col. 15, lines 44-46) and it also suggests administration of the bone marrow cell secretions (col. 15, line 57 and col. 17, line 11

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to administer the bone marrow stem cell secretions to the ischemic hear with a reasonable expectation of success in improving cardiac function as taught and/or suggested by US 7,097,832. One of skill in the art would have been motivated to administer the bone marrow stem cell secretions for the benefits in promoting new blood vessel

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growth and restoring function of ischemic heart as taught and/or suggested by US 7,097,832.

Thus, the claimed invention as a whole was clearly *prima facie* obvious, especially in the absence of evidence to the contrary.

The claimed subject matter fails to patentably distinguish over the state art as represented by the cited references. Therefore, the claims are properly rejected under 35 USC § 103.

Response to Arguments

Applicant's arguments filed 12/15/2006 and 10/27/2006 with respect to the new claims have been considered but are moot in view of the new ground(s) of rejection. The Declaration by Hani Sabbah filed on 12/15 2006 has been noted but it does not contain any data for consideration.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vera Afremova whose telephone number is (571) 272-0914. The examiner can normally be reached from Monday to Friday from 9.30 am to 6.00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber, can be reached at (571) 272-0925. The fax phone number for the TC 1600 where this application or proceeding is assigned is (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology center 1600, telephone number is (571) 272-1600.

Vera Afremova, AU 1657

February 28, 2007



VERA AFREMOVA

PRIMARY EXAMINER